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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/663,320	09/15/2000	Gavin C. Hirst	BBC-081/A	3710

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EXAMINER	
KIFLE, BRUCK	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 07/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/663,320	HIRST ET AL.	
	Examiner	Art Unit	
	Bruck Kifle, Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35,37-40 and 44-88* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35, 37-40 and 44-88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/17/04 has been entered.

Claims 1-35, 37-40 and 44-88 are pending in this application.

Claim Rejections - 35 USC § 112

Claims 1-35, 37-40 and 44-88 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

i) In the definition of Z^{110}, the term "alkyl" is missing following "(C_1-C_6)." Also in this definition the substituents on the amino group and phenyl are not known. See also definition of Z^{111}. The term "alkyl" is missing in Z^{105}, Z^{101} (7 occurrences) and Z^{200} as well.

ii) Claim 46 depends on cancelled claim 36. Claim 48 depends on claim 46, claim 49 depends on claim 48 and claim 50 depends on claim 46. These claims have not been further examined. Deletion is required.

Claims 33-35, 37-40, 44, 47 and 51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are drawn to a variety of methods. The basis of this

rejection is the same as given in the previous office action and is incorporated herein fully by reference.

Regarding the method of inhibiting one or more protein kinase activity, Applicant's arguments have been fully considered but not found persuasive. Applicant's are directed to the instant specification wherein is taught that there are over 400 protein kinases that vary widely. Therefore, inhibiting any protein kinase activity in any patient does not give any guidance to one skilled in the art how to use the instant claims because the specification fails to teach any benefit to be gained from such actions.

Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The list of conditions to be treated in claim 40 includes conditions such as leukemia, which is a class of hundreds of different diseases; HIV, which is so far only treatable with compounds which interfere with he life cycle of the virus; protozoa, which is not a condition; trauma, which includes all kinds of trauma from car accidents to emotional trauma; retinopathy, which is any eye disease; sarcoma, which is a broad category of cancers not related to each other; chronic retinal detachment, which is not treated pharmacologically but surgically; etc.

The notion that simply inhibiting one or more protein kinase activity will enable a whole list of unrelated disorders is not substantiated. Where the utilities are unusual or difficult to treat, such as, multiple sclerosis, the examiner has authority to require evidence that tests relied on are

reasonably predictive of in vivo activity by those skilled in the art, See for example, In re Ruskin 148 USPQ 221; Ex parte Jovanovics 211 USPQ 907 and MPEP 2164.05(e).

The scope of uses embraced by these claims are not remotely enabled based solely on instant compounds ability to inhibit one or more protein kinase activity.

The how to use portion of the statute has not been addressed. This means that Applicants must teach the skilled practitioner, in this case a physician, how to treat a given subject. The physician clearly must know what disease and what symptoms are to be treated. In a case concerning the patentability of compounds with "good effects against a wide range of insects" *In re LORENZ AND WEGLER*, 134 USPQ 312 U.S. Court of Customs and Patent Appeals upheld the rejection of compound claims, noting that "[a]ppellants are seeking a seventeen year monopoly. We would remind them that if they have in truth invented something which promotes the progress of science and the useful arts, then in exchange for a patent grant they must make a full and complete disclosure of their invention, leaving nothing to speculation or doubt. That Congress so intended is evident from the strong and comprehensive language of Section 112 which appellants here have failed to satisfy." In this case, Applicants have not provided what is being treated by claim 33, who the subject is, how one can identify said subject (i.e. how one can identify the patient), given no specific dose, given no specific dosing regimen, given no specific route of administration, and do not specify what diseases or symptom they intend to treat.

In a case, *In re MOUREU AND CHOVIN*, 145 USPQ 452, concerning the patentability of antitubercular compounds, The U.S. Court of Customs and Patent Appeals held "[i]t is therefore clear that those skilled in the art who desire to use the products of the invention for medicinal purposes would find it necessary to engage in extensive experimentation to determine what

would be the effective and safe manner of using the products as medicines for the suggested purposes and to determine the dosages to be avoided because lethal or ineffective. Both the examiner and the board recognized that compliance with section 112 does not necessarily require specific recitations of use if the method of using is inherent in the description of the compound, In re Nelson, 47 CCPA 1031, 280 F.2d 172, 126 USPQ 242. The board held, however, that a bald assertion that the claimed compounds possess antitubercular activity would not indicate to those skilled in the medical arts the manner of effectively using the compounds."

As the Supreme Court said in *Brenner v. Manson*, 148 USPQ at 696: "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." As U.S. Court of Customs and Patent Appeals stated *In re Diedrich* 138 USPQ at 130, quoting with approval from the decision of the board: "We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates."

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27

USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Claims 1-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to the invention. The specification is not adequately enabling for the scope of the compounds claimed. Only one compound has been made. This does not give a reasonable assurance that all, or substantially all of the compounds that could be made are useful. The claims are not drawn in terms of a recognized genus but are directed to a more or less artificial selection of compounds.

Also, see In re Surrey 151 USPQ 724, regarding sufficiency of a disclosure for a Markush group, and MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the instant pharmaceutical arts. Note in Surrey, in which testing done on a group of homogeneous compounds having the same core was deemed NOT sufficient to support claims to various hetero groups of a much narrower range than is being claimed herein and located at only one position in the formula. Applicants have made a single compound. The instant scope, however, is enormous (in the billions of compounds); therefore one compound within its scope is not remotely representative of such a scope. See MPEP 2164.03.

There is no reason why a claim drawn in this way should not be limited to those compounds which are shown to be useful. An Applicant is not entitled to a claim for a large group of compounds merely on the basis of a showing that a single compound is useful and a general suggestion of a similar utility in the others.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-35, 37-40 and 44-88 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Altmann et a. (WO 97/49706). The basis of this rejection is the same as given in the previous office actions and is incorporated herein fully by reference. The reference teaches a generic group of substituted 7-amino-pyrrolo[3,2-d]pyrimidine derivatives which embraces applicants' claimed compounds.

The instant claims are enormous; they easily embrace billions of compounds and, therefore, read on obvious as well as non-obvious subject matter. For example, consider the compound of Example 72 on page 25 of the reference. This compound has a hydroxyl group substituted at the 4-position of the phenyl group at R_1. One skilled in the art would be motivated to modify this prior art compound and arrive at the instant claims (where, for example, R_1 is phenyl, substituted at the 4-position by A-Z^{100}) because the reference teaches the equivalence of substituted aryl groups (listed on pages 3-4) as the most especially preferred compounds (see page 8, 3rd paragraph). A claim is unpatentable if only one embodiment within its scope is unpatentable.

The closest prior art compound is that of Example 72 on page 35. This prior art compound differs from the sole compound Applicant's have exemplified by having a 4-Ph-OH substituent over the 4-Ph-OPh group of the instant compound at R_1. Applicants need to show that their compounds have superior and/or unexpected properties over the prior art compounds.

Applicants have submitted copies of several related applications. Applicants are required to maintain a clear line of demarcation between the applications. See MPEP § 822. Applicants have still not responded to this request.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruck Kifle, Ph.D. whose telephone number is 571-272-0668. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund J. Shah can be reached on 571-272-0674. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Bruck Kifle, Ph.D.
Primary Examiner
Art Unit 1624

BK
June 25, 2004